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PATENT

F¹
9 said cell is detectable, and wherein if said first indicator component is an antibiotic
10 resistance marker, said second indicator component is not an antibiotic resistance marker.

F²
1 10 ~~16~~. (Amended) A method of screening for the integration of a DNA
2 construct into a target gene having restricted expression in a mouse, said method
3 comprising:
4 (i) transforming a mouse ES cell with a first DNA construct encoding a
5 first indicator component linked to a promoter having restricted expression in a mouse,
6 wherein DNA encoding the first indicator component is separated from said promoter by
7 a sequence of DNA which prevents transcriptional control by said promoter over the
8 DNA encoding the first indicator component;
9 (ii) transforming the cell of (i) or a descendent of the cell by operably
10 integrating into the cell's genome, a second DNA construct comprising DNA encoding a
11 second indicator component not operably linked to a transcription control element;
12 (iii) producing tissue or specialized cells of (ii); and
13 (iv) monitoring the tissue or specialized cells of (iii) for a detectable
14 indicator resulting from both the first and second indicator components indicative of
15 integration of the second DNA construct into a gene having restricted expression,
16 wherein in the second DNA construct, the second indicator component is a recombinase
17 capable of removing the sequence of DNA preventing transcriptional control in the first
18 DNA construct; and,
19 wherein said monitoring is for cells in which the first indicator component
20 is expressed under the transcriptional control of the promoter having restricted
21 expression.

REMARKS

With entry of this amendment, claims 1, 3-6, 9, 12, 13, and 15-19 are
pending in the application. Pursuant to the telephone conversation between the Examiner